

REMARKS

The Official Action of December 29, 2005, and the prior art relied upon therein have been carefully studied. The claims in the application are now claims 1-9 and 11, and these claims define patentable subject matter warranting their allowance. Applicant accordingly respectfully requests favorable reconsideration and allowance.

Acknowledgement by the PTO of the receipt of applicant's papers filed under Section 119 is noted.

Regarding paragraph 2 on page 2 of the Official Action under the heading "Priority", the amendment suggested to bring this information up to date has been made above. Otherwise, and for the record, the priority and benefit information originally set forth is adequately presented in both the Application Data Sheet (ADS) and the present application as filed. However, if the Examiner notices any error, advising applicant would be appreciated.

As regards paragraph 4 on page 2 of the Official Action under the heading "Information Disclosure Statement", applicant is unaware of any references mentioned in this specification which have not also been presented in an IDS.

Again, if applicant has overlooked any such reference, feedback from the Examiner would be appreciated.

Claims 1-11 have been rejected under the second paragraph of section 112. The rejection is respectfully traversed.

First, claim 1 has been amended above in the preamble to make more clear that what is being diagnosed is "the risk of" spontaneous abortion, as is absolutely clear from applicant's specification.

In addition, claim 1 has been amended by adding explicitly a second step which is clearly at least implicit in claim 1 as originally filed. The key disclosure relating to the use of antibodies according to the present invention to diagnose the risk of spontaneous abortion is to be found at page 4, lines 2-7.

Withdrawal of the rejection is in order and is respectfully requested.

Claims 1-7 have been rejected as obvious under Section 103 from Barquinero et al, reference AC (Barquinero) in view of O'Neill USP 4,879,285 (O'Neill). The rejection is respectfully traversed.

The claims of the present application relate to a method of diagnosing the risk of spontaneous abortion, by

determining the levels of antibodies to PAF (aPAF), and related antibodies, in a patient.

The PTO correctly accepts that Barquinero does not teach that antibodies to PAF (i.e. aPAF) can be used to evaluate the risk of spontaneous abortion. However, the PTO alleges that O'Neill in combination with Barquinero makes this method obvious. With respect, the such allegation appears to be based on a misunderstanding of the nature of the biological processes underlying the present invention.

Thus, O'Neill relates to fertility control and proposes that aPAF could be used as a *contraceptive*. By contrast, the present invention relates to diagnosing the risk of *spontaneous abortion*. As explained in more detail below, the biological processes underlying contraception and spontaneous abortion are *not the same*. Therefore, the person of ordinary skill in the art would not take the teaching of O'Neill as an indication that the risk of spontaneous abortion could be determined by assessment of the levels of aPAF in a sample of body fluid.

The key development reported in O'Neill is that PAF is identified as being important in the step in the early cell division of a fertilised embryo (for the 1-cell to 2-cell stage (Column 2, lines 58-60), and also in the step of implantation of the fertilised embryo in the uterus (Column 7,

lines 41-46). O'Neill reports that increased levels of PAF can enhance the rate at which fertilised embryos become implanted in the uterus, and thus can increase fertility (Columns 1-2). PAF is said to be key for mammalian implantation around 2-7 days after fertilisation (6 days in humans) (Column 2, lines 43-45).

O'Neill also proposes a method of reducing fertility in a female mammal by *"artificial inhibition of PAF-mediated pathways involved in embryo cell division and/or implantation"* (Column 3, lines 15-16). Several different types of inhibitors are proposed, one of which is antibodies to PAF (Column 3, lines 33-34).

However, O'Neill teaches that antibodies to PAF are less preferred inhibitors because *"high concentrations of, for example antibodies, are needed in the system to overcome the localised increase of embryo-derived PAF"* (Column 3, lines 43-46).

So, to recap, O'Neill teaches that -

- PAF is key at the very early stages of embryo cell division and implantation; and
- Cell division and embryo implantation can be reduced by artificially reducing PAF levels, but that antibodies to PAF are not preferred as inhibitors

because high levels of are required to counteract local increases in embryo-derived PAF.

O'Neill says absolutely nothing about naturally occurring levels of antibodies to PAF ("aPAF"). There is no teaching in O'Neill that natural variation in the levels of endogenous aPAF would, in any way, affect levels of embryo cell division and implantation, nor would the person skilled in the art expect them to do so, particularly given the teaching at Column 3, lines 42-46 that *"high concentrations of, for example antibodies, are needed in the system to overcome the localised increase of embryo-derived PAF"*. In view of this, the person of ordinary skill in the art would expect that the only way to influence embryo division and implantation with aPAF would be to *artificially* generate very high levels of aPAF local to the embryo.

There is absolutely no teaching or suggestion in O'Neill that one should assess the *endogenous* levels of aPAF in order to determine whether an individual female mammal is likely to be fertile, nor would the person skilled in the art expect that endogenous levels of aPAF could be *naturally* so high as to achieve the high levels referred to in O'Neill as being necessary to inhibit the beneficial effect of localised embryo-derived PAF on the early stages of embryo cell division

and uterine implantation. The PTO has extrapolated O'Neill well beyond its teachings.

O'Neill is completely silent on the clinical significance of *endogenous levels* of aPAF, and would not motivate the person skilled in the art to assess them at all.

Furthermore, even if the person skilled in the art did consider O'Neill to be a teaching that one should measure naturally occurring endogenous aPAF levels to assess fertility (which applicant respectfully denies), nevertheless O'Neill suggests that PAF and aPAF levels are only relevant to the early stages of embryo cell division (*"for the development of the 1-cell fertilised embryo to the 2-cell stage"*; column 2, lines 58-60) and implantation in the uterus.

By contrast, the present invention relates to a method of determining the risk of spontaneous abortion. Spontaneous abortion (otherwise known as "miscarriage") involves the expulsion of a foetus from the womb of a pregnant female (for example, see the definitions of abortion and miscarriage from The New Oxford Dictionary of English; extracts enclosed - both refer to expulsion of the foetus). There should be no doubt that a foetus is formed at a considerably later stage of pregnancy than the first few rounds of embryonic cell division and uterine implantation.

Applicant does not expect that any documentary support is necessary to substantiate this fact, but nevertheless enclosed please find an extract of the text book "Biological Science 2" from which it is clear (see page 761, section 20.3.7) that a human embryo is referred to as a foetus from around the third month of pregnancy - this is clearly much later than the period around 2-7 days after fertilisation (6 days in humans) in which O'Neill teaches PAF to be key for mammalian implantation (O'Neill, Column 2, lines 43-45).

Thus the method of the present application relates to the determination of risk termination of pregnancy at a considerably later stage than the processes of early embryo cell division and implantation as discussed in O'Neill. In fact, by definition, spontaneous abortion can only occur after an embryo has undergone early cell division and has been implanted in the uterus and, thus, at a stage of development that is much later than is considered by O'Neill to be relevant to PAF and aPAF levels.

It is clear that O'Neill is solely concerned with the role of PAF, and artificially introduced antagonists thereof, in the early stages of embryo cell division and embryo implantation. The O'Neill document is completely silent on the role of PAF and, more particularly, the implications of the endogenous levels of aPAF, at the later

stages of pregnancy during which spontaneous abortion of a fetus can occur. There is absolutely nothing in O'Neill that would lead a person of ordinary skill in the art to expect that endogenous levels of aPAF would be a marker of the risk of spontaneous abortion in a female mammal.

So, to summarize the above comments -

- O'Neill does not suggest that endogenous levels of aPAF could be of any clinical significance to fertility at all (indeed, O'Neill suggests that aPAF can only become clinically significant if raised to an *artificially* high level, local to the embryo), and so O'Neill does not motivate the person skilled in the art to determine *endogenous* levels of aPAF for any reason; and
- Even if the person skilled in the art were to be motivated by O'Neill to determine the endogenous levels of aPAF in a patient (for which applicant can see no reason), then nevertheless O'Neill teaches that PAF and aPAF could have clinical significance for a different biological process than claimed in the present invention (viz. early stage embryo cell division and implantation, rather than spontaneous abortion of a fetus which can only occur at a later stage of pregnancy) and so the person skilled in the art would not be motivated to use



the measurement of endogenous aPAF levels to assess the risk of spontaneous abortion.

To conclude, it is clear that O'Neill does not compensate for the deficiency in the teaching of Barquinero. Neither of these documents makes it obvious to the person skilled in the art that antibodies to PAF (i.e. aPAF) can be used to evaluate the risk of spontaneous abortion. As both references are lacking in part in the same respect, it follows that no combination of these references could possibly reach the claimed subject matter, even if such combination were obvious, respectfully denied.

Withdrawal of the rejection is in order and is respectfully requested.

Claims 8-11 have been rejected as obvious under Section 103 from Barquinero in view of O'Neill and further in view of Karasawa et al, reference AH (Karasawa). This rejection is respectfully traversed.

First, as pointed out above, both Barquinero and O'Neill, even if obviously combined (contrary to applicant's position), could not reach the subject matter of claim 1, let alone the subject matter of the dependent portions of any of claims 8-11 which depend from and thus incorporate the subject matter of claim 1. Karasawa has not been cited to make up for

the deficiencies of the proposed combination of Barquinero and O'Neill as explained above, and certainly does not do so.

Karasawa is totally silent on the possibility of any clinical significance between the levels of antibodies to PAF and PAF-related molecules phosphocholine, phosphorylcholine and lysophosphatidylcholine and the risk of spontaneous abortion.

Furthermore, the PTO has, with respect, misunderstood the teaching of Karasawa. It does not teach a method of measuring levels of any types of antibodies; on the contrary, it teaches a method of measuring the levels of PAF in a sample and uses, as a tool, a preparation of antibodies that comprises anti-PAF antibodies ("aPAF").

The test of Karasawa uses serum obtained from a PAF-immunised rabbit. This serum contains a mixture of different antibodies that contains, amongst others, antibodies to PAF. Karasawa teaches that such serum is used to detect PAF in a sample. Page 1127, second column, first paragraph of the "results" section, reports that *"For the radioimmunoassay, we used antiserum collected after the fourth injection"*.

The radioimmunoassay of Karasawa involves measuring the level of PAF in a sample by measuring the ability of any PAF in that sample to compete with radio-labelled PAF to bind to antibodies in the rabbit antiserum. It is therefore seen

that this method does not measure the levels of any antibodies, much less the levels of antibody to phosphocholine, phosphorylcholine or lysophosphatidylcholine, in the collected antiserum. On the contrary, the antiserum that was collected was used by Karasawa et al as a tool in the quantification of PAF in a sample of choice.

Since the collected antiserum used in the radioimmunoassay of Karasawa contained a *mixture* of antibodies from the rabbit, some (in fact most) of the antibodies in the sample would not be specific to PAF. Accordingly, competitive inhibition of binding of the radio-labelled PAF to the antiserum, by compounds in the biological sample being tested, could potentially be due to the presence of an antibody in the antiserum that has a non-specific binding affinity both for PAF and also other molecules in the biological sample tested, and those other molecules being able to compete with, and inhibit the binding of, radio-labelled PAF to this non-specific antibody in the antiserum. In that case, the radioimmunoassay clearly could not be used to reliably quantify the level of PAF in a sample.

Because of this potential problem, the authors of the Karasawa publication wanted to check that they were observing a specific binding of PAF in the competitive radioimmunoassay. To do this, they compared the binding of

the antiserum to other PAF-like molecules. Page 1128, second column, lines 2-8 reports that:

*Cross-reactivity studies of the antiserum revealed a high specificity for PAF. Choline-containing phospholipids such as lysoPAF, lecithin or lysoPC did not cross-react with PAF antiserum (Table 1) (emphasis added).*

In other words, Karasawa et al satisfied themselves that the antiserum sample that they obtained could be reliably used to measure the level of PAF in a sample, because the antiserum did not contain any antibodies that would non-specifically bind both PAF and other PAF-like molecules.

Likewise, in Barquinero, page 57, left hand column, the authors reported that anti-PAF antibodies that had been affinity purified using PAF as a ligand did not cross react with phosphatidylcholine and other phospholipids (see section entitled "Affinity purified anti-PAF"). The section that follows (entitled "Inhibition studies") reports that the binding of PAF to affinity-purified IgM anti-PAF antibodies could be inhibited by the presence of phosphatidylcholine, which suggests that some anti-PAF antibodies can also bind to phosphatidylcholine, but that section also reports that "PAF produced the highest inhibition" which tells the skilled artisan reader that the best way to capture such antibodies is to use PAF as an affinity ligand.

Therefore, the teaching of both Karasawa and Barquinero is that, generally, anti-PAF antibodies do not bind to other PAF-like molecules and, where they do (such as in the case of the binding of IgM anti-PAF antibodies to phosphatidylcholine, as discussed in Barquinero) then such antibodies still bind more strongly to PAF itself.

Accordingly, in light of the teaching of Barquinero, either alone or in combination with the teaching of Karasawa, the skilled person is motivated to use PAF alone to determine the presence of anti-PAF antibodies in a sample.

There is no motivation provided in either Barquinero or Karasawa to test a sample of body fluid for the presence of antibodies other than anti-PAF antibodies (because there is no indication that such antibodies exist, much less that they have any clinical significance). Accordingly, in light of the teaching of Barquinero, alone or in combination with Karasawa, the skilled person would only be motivated to determine the presence of anti-PAF antibodies in a sample from a patient and, as discussed above, the teaching of Barquinero is then that, to the extent that one wishes to determine the presence of anti-PAF antibodies, one should use PAF as a ligand to capture such antibodies.

Therefore, it would not have been obvious, in light of these prior art documents, to use any of phosphocholine,

phosphorylcholine or lysophosphatidylcholine to determine the levels, in a patient's sample, of antibodies that bind to these compounds, much less to do so for the purposes of determining the risk of spontaneous abortion.

Furthermore, phosphocholine, phosphorylcholine and lysophosphatidylcholine are smaller, more simple molecules than PAF, and accordingly comprise fewer epitopes than PAF. As a result, the use of phosphocholine, phosphorylcholine and/or lysophosphatidylcholine as a ligand provides the user with the ability to bind a more specific group of antibodies. This further advantage was not appreciated in the cited art.

In summary -

- O'Neill does not suggest that endogenous levels of aPAF could be of any clinical significance to fertility at all (indeed, O'Neill suggests that aPAF can only become clinically significant if raised to an *artificially* high level, local to the embryo), and so the document does not motivate the person skilled in the art to determine *endogenous* levels of aPAF for any reason.
- Even if the person skilled in the art were to be motivated by O'Neill to determine the endogenous levels of aPAF in a patient (for which applicant can see no reason), then nevertheless O'Neill teaches that PAF and aPAF could have clinical significance for a different

biological process than claimed in the present invention (viz. only early stage embryo cell division and implantation, rather than spontaneous abortion of a foetus which can only occur at a later stage of pregnancy), and so the person skilled in the art would not be motivated to use the measurement of endogenous aPAF levels to assess the risk of spontaneous abortion. There is certainly no suggestion in O'Neill that endogenous levels of antibodies to phosphocholine, phosphorylcholine and/or lysophosphatidylcholine could have any clinical significance to the risk of spontaneous abortion.

- The PTO has accepted that Barquinero also does not motive the person skilled in the art to use the measurement of endogenous aPAF levels to assess the risk of spontaneous abortion. Again, it is clear that there is no suggestion in Barquinero that endogenous levels of antibodies to phosphocholine, phosphorylcholine and/or lysophosphatidylcholine could have any clinical significance to the risk of spontaneous abortion.
- Karasawa is silent on the clinical significance of antibodies to PAF and/or antibodies to phosphocholine, phosphorylcholine and/or lysophosphatidylcholine. Moreover, in direct contrast to the suggestion in the

rejection, Karasawa does not teach a method of measuring antibodies at all; rather it teaches a method of measuring PAF, that method using a preparation of antibodies. One can infer from the teachings of Karasawa and Barquinero that, if one did wish to capture antibodies to PAF then one should use PAF, as a ligand and not one of phosphocholine, phosphorylcholine and/or lysophosphatidylcholine. Thus, even if the person skilled in the art did look to combine the teaching of Barquinero, O'Neill and Karasawa, then the skilled person would be led away from the invention as alleged for in Claims 8, 9 and 11.

To conclude, it is clear that Karasawa does not compensate for the deficiencies in the teaching of any possible combination of Barquinero and O'Neill. None of the documents makes it obvious to the person skilled in the art that antibodies to PAF (i.e. aPAF) and/or antibodies to phosphocholine, phosphorylcholine and/or lysophosphatidylcholine can be used to evaluate the risk of spontaneous abortion.

Accordingly, the claims of the present are clearly non-obvious over Barquinero, O'Neill, and Karasawa, alone or in combination.



Appln. No. 10/814,194  
Amd. dated March 29, 2006  
Reply to Office Action of December 29, 2005

Withdrawal of the rejection is in order and is respectfully requested.

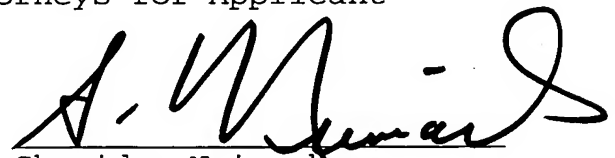
The prior art documents of record and not relied upon by the PTO have been noted, along with the implication that such documents are deemed by the PTO to be insufficiently material to warrant their application against any of applicant's claims.

Applicant believes that all issues raised in the Office Action have been addressed above in a manner favorable to allowance of the present application. Accordingly, applicant respectfully requests favorable reconsideration and early formal allowance.

Respectfully submitted,

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# The New Oxford Dictionary of English

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## aborigine

**aborigine** /əbərɪˈdʒiːn/ ► noun a person, animal, or plant that has been in a country or region from earliest times.

■ (Aborigine) an aboriginal inhabitant of Australia.  
- ORIGIN mid 19th cent.: back-formation from the 16th-cent. plural *aborigines* 'original inhabitants' (in classical times referring to those of Italy and Greece), from the Latin phrase *ab origine* 'from the beginning'.  
[USACF] See also *Aboriginal*.

**aborning** /əˈbɔːrɪŋ/ ► adverb chiefly N. Amer. while being born or produced: *the idea died aborning*.

- ORIGIN 1930s: from *a-* 'in the process of' + *born*, verbal noun from *born* (North American dialect usage) 'to be born'.

**abort** ► verb (with obj.) 1 carry out or undergo the abortion of (a fetus).

■ [no obj.] (of a pregnant woman or female animal) have a miscarriage. With loss of the fetus. ■ [no obj.] Biology (of an embryonic organ or organism) remain undeveloped; fail to mature.

2 bring to a premature end because of a problem or fault: *the flight crew aborted the take-off*.

► noun informal or technical an act of aborting a flight, space mission, or other enterprise: *an abort because of bad weather*.

3 an aborted enterprise or undertaking: *I've wasted almost a year on an abort*.

- ORIGIN mid 16th cent.: from Latin *abortiri* 'miscarry', from *ab-* 'away, from' + *ortiri* 'be born'.

**abortifacient** /əˈbɔːrɪfəʃ(ə)nt/ ► adjective (chiefly of a drug) causing abortion.

► noun an abortifacient drug.

**abortion** ► noun 1 (mass noun) the deliberate termination of a human pregnancy, most often performed during the first 28 weeks: concerns such as *abortion and euthanasia* | [count noun] *illegal abortions*.

2 the expulsion of a fetus from the womb by natural causes before it is able to survive independently. ■ Biology the arrest of the development of an embryo, typically a seed or fruit.

3 an object or undertaking regarded as unpleasant or badly made or carried out.

- ORIGIN mid 16th cent.: from Latin *abortio(n)-*, from *abortiri* 'miscarry' (see *ABORT*).

**abortionist** ► noun a person who carries out abortions (often applied to some-one not working in a hospital, or used to convey disapproval of abortion).

**abortion mill** ► noun informal, chiefly N. Amer. used pejoratively by opponents of abortion to refer to an abortion clinic.

**abortion pill** ► noun informal a drug which can induce abortion, especially mifepristone.

**abortive** ► adjective 1 failing to produce the intended result: *she made two abortive attempts at suicide*.

2 Biology, dated (of an organ or organism) rudimentary; arrested in development: *abortive medusae*.

3 Medicine (of a virus infection) failing to produce symptoms.

4 not causing or resulting in abortion.

- DERIVATIVES *abortively* adverb.

- ORIGIN Middle English (as a noun denoting a stillborn child or animal): via Old French from Latin *abortivus*, from *abortiri* 'miscarry' (see *ABORT*).

**abortus fever** /əˈbɔːrɪtəs/ ► noun (mass noun) the commonest form of undulant fever in humans.

■ A type of disease is caused by the bacterium *Brucella abortus*, which is also the chief cause of brucellosis in cattle.

- ORIGIN 1920s: from Latin *abortus* 'miscarriage'.

**ABO system** ► noun a system of four basic types (A, B, and O) into which human blood may be classified, based on the presence or absence of certain inherited antigens.

**Aboukir Bay, Battle of** /əˈbuːkɪr/ (also *Abukir Bay*) a naval battle in 1798 off Aboukir Bay at the mouth of the Nile, in which the British under Nelson defeated the French fleet. Also called **BATTLE OF THE NILE**.

**aboulia** ► noun variant spelling of *avolun*.

**abound** ► verb (no obj.) exist in large numbers or amounts: *rumours of a further scandal abound*.

■ [abounded in/with] have in large numbers or amounts: *this area abounded with carmen rice*.

- ORIGIN Middle English (in the sense 'overflow, be abundant'): from Old French *abunder*, from Latin

*abundare* 'overflow', from *ab-* 'from' + *undare* 'surge' (from *unda* 'a wave').

**about** ► preposition 1 on the subject of; concerning: *I was thinking about you* | *I asked him about his beliefs*.

2 so as to affect; there's nothing we can do about it. ■ [be about] be involved or to do with; have the intention of: *he's all about having fun*.

3 used to indicate movement within a particular area: *she looked about the room*.

4 used to express location in a particular place: *rugs strewn about the hall* | *he produced a knife from somewhere about his person*.

5 used to describe a quality apparent in a person: *there was a look about her that said everything*.

► adverb 1 used to indicate movement within an area: *men were floundering about* | *finding my way about*.

2 used to express location in a particular place: *there was a lot of flu about* | *a thief about in the hotel*.

3 (used with a number or quantity) approximately: *reduced by about 5 per cent* | *he's about 25*.

- PHRASES *about to do something* intending to do something or close to doing something very soon: *the ceremony was about to begin*. ■ *be not about to do something* be unwilling to do something: *he is not about to step down after so long*. ■ *be on about see ON*. ■ *how about see HOW*. ■ *just about see JUST*. ■ *know what one is about* informal be aware of the implications of one's actions or of a situation, and of how best to deal with them. ■ *what about see WHAT*.

- ORIGIN Old English *ambutan*, from *an* 'in, on' + *butan* 'outside of' (see *BUT*).

**about-face** ► noun & verb chiefly N. Amer. another term for *about-turn*.

**about-turn** /əˈbaʊtˌtɜːn/ ► noun (chiefly in military contexts) a turn made so as to face the opposite direction: *he did an about-turn and marched out of the tent*.

2 a complete change of opinion or policy: *the government made an about-turn over the bill*.

► verb [no obj.] turn so as to face the opposite direction.

► exclamation (about turn) (in military contexts) a command to make an about-turn.

- ORIGIN late 19th cent. (originally as a military command): shortening of *right about turn*.

**above** ► preposition 1 in extended space over and not touching: *a display of fireworks above the town* | *a cable runs above the duct*.

2 extending upwards over: *her arms above her head*. ■ higher than and to one side of; overlooking: *in the hills above the capital* | *on the wall above the altar*.

3 at a higher level or layer than: *from his 'des res' above the corner shop* | *bristles above both eyes*.

4 higher in grade or rank than: *at a level above the common people*. ■ considered of higher status or worth than: *too good for the married above her* | *above reproach*. ■ in preference to: *the firm usually chose trains above car sales*. ■ at a higher volume or pitch than: *above a whisper* | *the doorbell went unheard above the din*.

5 higher than (a specified amount, rate, or normal): *above average* | *above freezing* | *above sea level* | *the unemployment rate will soar above its present level*.

► adverb at a higher level or layer: *place a quantity of mud in a jar with water above*.

2 higher in grade or rank: *an officer of the rank of superintendent or above*. ■ higher than a specified amount, rate, or norm: *boats of 21 ft or above*. ■ (in printed text) mentioned earlier or further up on the same page: *the two cases described above* | *see above left* | (as adj.) *the above address* | (as noun) *since writing the above, I have reconsidered*.

- PHRASES *above all (also) more so than anything else*: *he was concerned above all to speak the truth*. ■ *above oneself* conceited; arrogant: *from above from overhead*: *brandish* raised from above. ■ from a position of higher rank or authority: *maz culture is imposed from above*. ■ not to be above the capability of stooping to (an unworthy act): *he was not above practical jokes over said above see OVER*.

- ORIGIN Old English *abufan* (as an adverb), from *a-* 'on' + *bifan* (from *bi* 'by' + *ufan* 'above').

**above board** ► adjective & adverb legitimate, honest, and open: (as adj.) *certain transactions were not totally above board* | (as adv.) *the accountants acted completely above board*.

**ab ovo** /əb ˈʊvʊ/ ► adverb from the very beginning.

- ORIGIN Latin, literally 'from the egg'.

**Abb** ► abbreviation for Archbishop.

**abracadabra** ► exclamation a word said by conjurers when performing a magic trick.

► noun (mass noun) informal the implausibly easy

performance of difficult feats: *the erosion of profit was a marvellous bit of abracadabra*.

■ language used to give the impression of arcane knowledge or power: *I get so fed up with all the mumbo jumbo and abracadabra*.

- ORIGIN late 17th cent. (as a mystical word conjured and used as a charm to ward off illness): from Latin, first recorded in a 2nd-cent. poem by (Serenus) Sammonicus, from a Greek base.

**abrade** /əˈbreɪd/ ► verb (with obj.) scrape or wear away by friction or erosion: *a landscape slowly abraded by fine, stinging dust*.

- DERIVATIVES *abraded* noun.

- ORIGIN late 17th cent.: from Latin *abradere*, from *ab-* 'away, from' + *radere* 'to scrape'.

**Abraham** /ˈæbrəhɑːm/ (in the Bible) the Hebrew patriarch from whom all Jews trace their descent (Gen. 11:27-25:10). In Gen. 22 he is ordered by God to sacrifice his son Isaac as a test of faith, command later revoked.

**Abraham, Plains of** see **PLAINS OF ABRAHAM**.

**Abrahams** /ˈæbrəhɑːmz/, Harold (pseudonym) (died 1978), English athlete. In 1924 he became the first Englishman to win the 100 metres in the Olympic Games. His story was the subject of the film *Charlo of Fire* (1981).

**abrasion** /əˈbreɪʃ(ə)n/ ► noun (mass noun) the process of scraping or wearing away: *the metal is resistant to abrasion*.

■ [count noun] an area damaged by scraping or wear: *away there were cuts and abrasions to the lips and jaw*.

- ORIGIN mid 17th cent.: from Latin *abrasio(n)-*, from the verb *abradere* (see *ABRADE*).

**abrasive** /ˈæbrəzɪv/ ► adjective (of a substance or material) capable of polishing or cleaning a hard surface by rubbing or grinding.

2 tending to rub or graze the skin: *the trees were abrasive to the touch*. ■ figurative (of sounds or music) rough: *the car's harsh, fast abrasive rhythms*. ■ figurative (of person or their manner) showing little concern for the feelings of others: *harsh, her abrasive and arrogant personal style won her few friends*.

► noun a substance used for grinding, polishing, or cleaning a hard surface.

- ORIGIN mid 19th cent. (as a noun): from Latin *abradere* 'abraded', from the verb *abradere* (see *ABRADE*).

**abrazo** /əˈbræzəʊ, əˈbræsoʊ/ ► noun (pl. -os) US & embrace.

- ORIGIN Spanish.

**abreact** /ˈæbrɪəkt/ ► verb (with obj.) Psychomally release (an emotion) by abstraction.

■ cause (someone) to undergo abstraction.

- ORIGIN early 20th cent.: back-formation from *ABREACTION*.

**abreaction** ► noun (mass noun) Psychomally the expression and consequent release of a previously repressed emotion, achieved through reliving the experience that caused it (typically through hypnosis or suggestion).

- DERIVATIVES *abreactive* adjective.

- ORIGIN early 20th cent.: from *ab-* 'away from' + *reaction*, translating German *Abreagierung*.

**abreast** ► adverb 1 side by side and facing the same way: *the path was wide enough for two people to walk abreast* | *they were riding abreast*.

2 alongside or level with something: *the cart came abreast of the Americans in their ride-down* | *the car broke as it drew abreast*.

3 figurative up to date with the latest news, ideas, or information: *keeping abreast of developments*.

- ORIGIN late Middle English: from *a-* 'in' + *BREAST*.

**abridge** ► verb (with obj.) (usu. be abridged) 1 shorten (a book, film, speech, or other text) without losing the content: *the cassette has been abridged from the original stories* | (as adj.) *abridged* a *condensed text of his speech*.

2 law curtail (a right or privilege).

- DERIVATIVES *abridgement* adjective, *abridger* noun.

- ORIGIN Middle English (in the sense 'deprive of') from Old French *abregier*, from late Latin *abbreviare* 'cut short' (see *ABBRIVIATE*).

**abridgement** (also *abridgment*) ► noun 1 shortened version of a larger work: *an abridgement of Shakespeare's Henry VI*.

2 law a curtailment of rights.

- ORIGIN late Middle English: from Old French *abregement*, from the verb *abregier* (see *ABREGIER*).

**abroad** ► adverb 1 in or to a foreign country or

**unworkable alliance or marriage.**  
**ORIGIN** mid 18th cent.: from *mis-* 'wrong' + *alliance*, on the pattern of French *métallier*.

**misallocate** ▶ verb (with obj.) fail to allocate (something) efficiently or fairly.  
**DERIVATIVES** misallocation noun.

**misandry** /mɪˈændrɪ/ ▶ noun (mass noun) the hatred of men (i.e. the male sex especially).  
**ORIGIN** 1940s: from Greek *mis-* 'hating' + *andros* 'man', on the pattern of *misogyny*.

**misanthrope** /mɪˈzænθrəʊp/ ▶ noun (also *misanthropist* /mɪˈzænθrəʊpɪst/) ▶ noun a person who dislikes humankind and avoids human society.  
**DERIVATIVES** misanthropic adjective, misanthropically adjective, misanthropically adverb.

**ORIGIN** mid 16th cent.: from Greek *misandros*, from *mis-* 'hating' + *anthropos* 'man'.

**misanthropy** /mɪˈzænθrəpi/ ▶ noun (mass noun) a dislike of humankind.  
**ORIGIN** mid 17th cent.: from Greek *misanthropia*, from *mis-* 'hating' + *anthropos* 'man'.

**misapply** ▶ verb (-less, -less) (with obj.) (usu. be misapplied) use (something) for the wrong purpose or in the wrong way.  
**DERIVATIVES** misapplication noun.

**misapprehension** ▶ noun a mistaken belief about or interpretation of something; people tried to exchange the vouchers under the misapprehension that they were book tokens.  
**DERIVATIVES** misapprehensive adjective.

**misappropriate** ▶ verb (with obj.) (of a person) dishonestly or unfairly take (something, especially money, belonging to another) for one's own use; she reports revealed that department officials had misappropriated funds.  
**DERIVATIVES** misappropriation noun.

**misbegotten** ▶ adjective badly conceived, designed, or planned; someone's misbegotten idea of an English country house.  
**ORIGIN** 16th cent.: as a term of abuse: you misbegotten hound! = wretch (of a child) illegitimate.

**misbehave** ▶ verb (no obj.) (of a person, especially a child) fail to conduct oneself in a way that is acceptable to others; behave badly.  
**ORIGIN** 16th cent.: from *mis-* 'wrong' + *behave* 'behave'.

**misbelief** ▶ noun a wrong or false belief or opinion; the misbelief that alcohol problems require a specialist response.  
**DERIVATIVES** misbehaviour noun.

**mischievous** ▶ adjective (of a person or their behaviour) causing or showing a fondness for causing trouble in a playful way; mixing up the signpost was a favourite pastime of the more mischievous pupils.  
**ORIGIN** 16th cent.: from Old French *meschever* 'to mix' + *meschever* 'to mix'.

**mischievousness** ▶ noun the quality or state of being mischievous.  
**DERIVATIVES** mischievously adverb, mischievousness noun.

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**ORIGIN** Middle English: from Old French *meschever* 'to mix' + *meschever* 'to mix'.

**ORIGIN** mid 19th cent.: formed irregularly from Latin *miscere* 'to mix' + *genus* 'race' = *miscellaneus*.

**miscellaneous** /mɪˈseɪlənɪəs/ ▶ adjective (of items or people gathered or considered together) of various types or from different sources; he picked up the miscellaneous papers in the in tray.  
**ORIGIN** 16th cent.: from Latin *miscellaneus* 'mixed', from *miscere* 'to mix' + *-us*, in earlier use the word also described a person as 'having various qualities'.

**miscellaneity** /mɪˈseɪlənɪti/ ▶ noun (pl. -ies) a group or collection of different items; a miscellaneity of the east was a miscellaneity of houses.  
**ORIGIN** 16th cent.: from French *miscellanée* (feminine plural), from Latin *miscellanea* (see *MISCELLANEA*).

**miscellaneous** ▶ adjective (of items or people gathered or considered together) of various types or from different sources; he picked up the miscellaneous papers in the in tray.  
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**misconception** ▶ noun a view or opinion that is incorrect because based on faulty thinking or understanding; public misconceptions about AIDS remain high.

**misconduct** ▶ noun (mass noun) 1 unacceptable or improper behaviour, especially by an employee or professional person: she was found guilty of professional misconduct by a disciplinary tribunal.  
 2 mismanagement, especially culpable neglect or duties.

**misconduct** ▶ verb 1 (misconduct oneself) behave in an improper or unprofessional manner.  
 2 (with obj.) mismanage (a business or a project).

**misconstruct** ▶ verb (with obj.) nm misconstruct (something).  
**DERIVATIVES** misconstruction noun.

**misconstrue** ▶ verb (misconstruing) (with obj.) interpret (something, especially a person's words or actions) wrongly; my advice was deliberately misconstrued.  
**DERIVATIVES** misconstruction noun.

**miscount** ▶ verb (with obj.) count (something) incorrectly.  
**ORIGIN** 16th cent.: from *mis-* 'wrong' + *count* 'count'.

**miscreant** /mɪˈskriːnt/ ▶ noun a person who behaves badly or in a way that breaks the law, especially a heretic.  
**ORIGIN** Middle English (as an adjective in the sense 'disbelieving'); from Old French *mescreant*, present participle of *mescreire* 'disbelieve', from *mes-* 'mis-' + *creire* 'believe' (from Latin *credere*).

**miscue** ▶ noun (in billiards and snooker) a shot in which the player fails to strike the ball properly with the cue.  
**ORIGIN** 16th cent.: from *mis-* 'wrong' + *cue* 'cue'.

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# BIOLOGICAL SCIENCE 2

## Systems, Maintenance and Change

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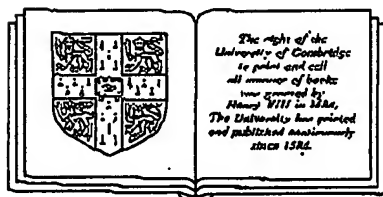
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pressure of the maternal circulation. It cannot function, however, as an immunological barrier; and since the foetus carries paternal genes it will produce antigens foreign to the mother who will produce antibodies against them. The mechanisms accounting for the remarkable ability of the foetus (or, in immunological terms, the homograft) to resist rejection for the 40 weeks of gestation is not known but is thought to involve the production of immune suppressive substances which circulate in the maternal plasma.

The continual passage of oxygen from mother to foetus is vital to the life and development of the foetus and this is ensured by the difference in affinity for oxygen between foetal and maternal haemoglobins as described in section 14.13.1.

The placenta is an endocrine organ whose major secretions are chorionic gonadotrophin, oestrogens, progesterone and human placental lactogen. The latter hormone stimulates mammary development in preparation for lactation. The site of secretion of all these hormones is the connective tissue of the chorion.

#### Sexual development in the embryo

The genetic sex of the embryo is determined at fertilisation by the sex chromosomes carried by the father's sperm, X in the case of a female and Y in the case of a male. Despite this, it would appear that the basic disposition of the human body is towards being female, largely as a result of the presence of an X chromosome in both sexes. In the early stages of embryonic development a pair of undifferentiated embryonic gonads, the genital ridges, and both rudimentary female and male reproductive systems develop in the embryo. As a result of this, all embryos are potentially bisexual up to the sixth week of development.

Recent investigations have revealed a possible mechanism whereby the sex chromosomes determine which of these systems is activated and lead to the phenotypic expression of the embryo's sex.

The X chromosome carries a gene, the *Tfm* gene (testicular feminisation gene) which specifies the production of an androgen-receptor protein molecule in the cells of the developing reproductive system. Since both male and female embryos carry at least one X chromosome, this molecule is present in both sexes.

The Y chromosome carries a gene called the Y-linked testis-determining gene specifying the production of a protein molecule, the H-Y antigen which stimulates the cells of the embryonic genital ridges to differentiate into seminiferous tubules and interstitial cells. Testosterone released into the embryonic circulatory system reacts with the androgen-receptor molecules in the target cells of the potential reproductive system. The androgen-receptor/testosterone complex formed passes to the nuclei where it activates genes associated with the development of the tissues. Testosterone will activate only those tissues which give rise to the male reproductive system and therefore an XY embryo will develop into a male foetus. The tissues of the potential female reproductive system are not activated

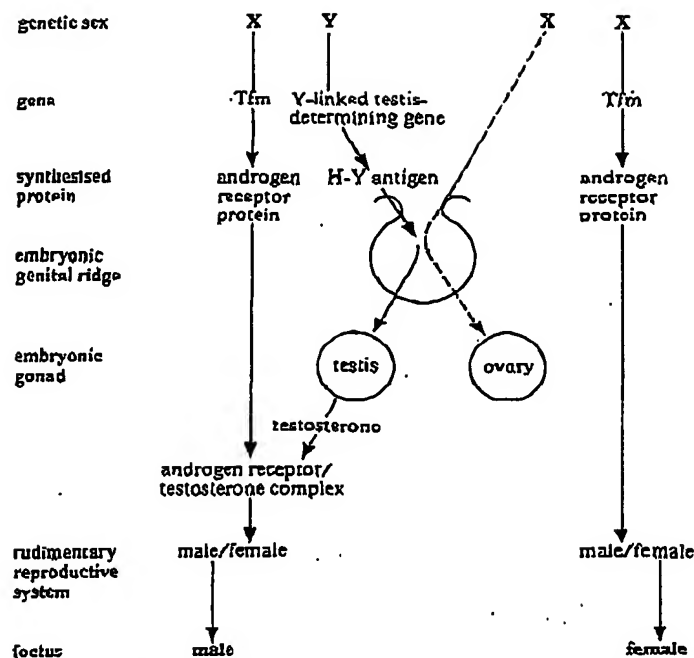


Fig 20.47 Summary diagram showing the events involved in the differentiation of the embryonic genital ridge and rudimentary reproductive system into the specific gonad and reproductive system of the foetus

and do not develop. In an XX embryo, the absence of testosterone allows the reproductive system to develop in its inherent direction towards that of female.

Thus it may be concluded that placental influences will direct the development of the embryo in the direction of a female unless diverted by a mechanism initiated by the Y chromosome. A summary of these events is shown in fig 20.47.

#### 20.3.7 Birth

From the beginning of the third month of pregnancy the human embryo is referred to as the foetus and it normally completes a total of 40 weeks of development, the gestation period, before birth occurs. Most of the major organs are formed by the twelfth week of pregnancy and the remainder of the gestation period is taken up by growth.

Throughout pregnancy oestrogen and progesterone are secreted in progressively greater amounts, first by the corpus luteum and then principally by the placenta. In the last three months of pregnancy oestrogen secretion increases faster than progesterone secretion and, immediately prior to birth, the progesterone level declines and the oestrogen level increases. The functions of these hormones in pregnancy are summarised in table 20.4.

It was thought that hormonal activities within the mother controlled the timing of birth but recent evidence obtained from research on several mammals has suggested there is a



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